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Attention deficits detected in cognitive tests differentiate between sleep apnea patients with or without a motor vehicle accident

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Short title: Cognitive impairment and risk of MVA in OSA

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Highlights

- Cognitive tests were assessed in OSA patients with or without previous MVAs
- For the first time objective MVAs and cognitive function in OSA have been assessed
- More lapses of attention and increased reaction time were seen in patients with MVA
- OSA severity and excessive sleepiness were not associated with MVAs

Abstract

Objectives Obstructive sleep apnea (OSA) is associated with an increased motor vehicle accident (MVA) risk. Conventional measures of OSA severity do not predict individual risk. Cognitive function tests have failed to incorporate outcomes in risk prediction. We aimed to identify markers of cognitive function for MVA risk prediction in OSA.

Methods OSA patients (n=114, 75% male, median age 51[43 – 61] years, Body-Mass Index (BMI) 30[27 – 33] kg/m^2, Apnea-Hypopnea Index 25[6 – 49] n/h, Epworth Sleepiness (ESS) score 11[8 – 16]) were recruited from a sleep laboratory. Two cognitive function tests, the Attention Network Test (ANT) and a modified OSLER test (GOSLING), were assessed.

Results OSA patients with (n=11) or without (n=103) a MVA record in the Swedish traffic accident registry were identified. In patients with a MVA, 64% were commercial drivers. In patients with a MVA history, more lapses (42[5 – 121] vs. 5[1 – 25], p=0.02) and fewer responses (238[158 – 272] vs. 271[256 – 277], p=0.03) to stimuli in the ANT were found. In the GOSLING, number of lapses was higher (29[10-97] vs. 7[2 – 19], p=0.01) and reaction time was longer (462[393 – 551] vs. 407[361 – 449] ms, p=0.05) OSA severity and ESS score poorly predicted MVAs (p>0.2).

Conclusions We have demonstrated that deficit in sustained attention, assessed by daytime neurocognitive function tests, was associated with MVA risk in OSA patients. We were unable to detect an association between MVA history and severity of OSA or the ESS score. The findings provide a rationale for further development of objective MVA risk assessment tools in OSA.

Keywords: Sleepiness; traffic risk; neurocognitive function; reaction time; accident registry; drowsy

1. Introduction

Obstructive sleep apnea (OSA) is characterized by episodes of repetitive upper airway collapse during sleep leading to recurrent hypoxia and micro arousals from sleep. Common clinical features of OSA include excessive daytime sleepiness (EDS)[1] and deficits in attention.[2, 3]

The prevalence of motor vehicle accidents (MVA) has been shown to be 2 to 3-fold higher in patients with OSA[4] and OSA treatment has been shown to be associated with a significant reduction of incident MVA.[5] Despite the strong association between OSA and MVA risk, the challenging task to identify individual patients at risk remains in clinical practice since MVA occur only in a minority of OSA patients.[6]

OSA severity in terms of apneic events failed to consistently predict MVA risk in a recent meta-analysis.[4, 7] EDS, operationalized by the Epworth Sleepiness Scale (ESS) score,[8] provided only weak prediction of risk.[7, 9] The Multiple Sleep Latency Test (MSLT) and the Maintenance of Wakefulness Test (MWT)[10] accurately define sleep propensity and capacity to maintain wakefulness during daytime, but their capacity in terms of MVA prediction has been debated.[11] Moreover, these tests are cumbersome and labor-intense and therefore less suitable for MVA risk assessment in clinical routine. Non-electroencephalography (EEG) based functional tests applied in the context of MVA risk prediction in OSA include driving simulators,[12, 13] real time driving, reaction time tests like the OSLER[14] and the Psychomotor Vigilance Test (PVT).[15] Deficits in attention in the general population are associated with impaired driving skills but, an association between such deficits and documented MVA has not previously been investigated in OSA, a condition associated with increased risk for neurocognitive impairment.

The aim of the current study was to retrospectively assess the possible association between poorer performance in two neurocognitive tests and MVA in a nationwide traffic accident registry in patients with OSA.

2. Material and Methods

2.1. Study population

The study cohort (n=114) was at the Sahlgrenska University Hospital Sleep Center. The patients were included from three sub-cohorts of patients comprising; 1) patients from a clinical OSA cohort (n=58); 2) subjects recruited from a pharmacotherapy study[16] in OSA (n=43); and 3) a study of public transport operators[17] diagnosed with clinically relevant OSA (n=13) (table 1). All patients were untreated and participated in a standardized neurocognitive test procedure in the research laboratory between the period 2006 and 2011. Data on gender and age, body mass index (BMI, kg/m^2), and ESS score were obtained. The study was approved by the regional ethical review board in Gothenburg. Oral and written informed consent was obtained from all study participants.

2.2. Assessment of daytime sleepiness and obstructive sleep apnea

The standardized Epworth Sleepiness Scale (ESS)[8] was used to define general daytime sleepiness. A score of ≥11 was considered as excessive daytime sleepiness (EDS).

Ambulatory polysomnography (PSG) was measured in 99 (87%) patients (Embla® A10, Colorado, USA) PSG recordings were analyzed according to the 2007 AASM criteria.[18] Polygraphy recording (PG, Embletta X10 system, Colorado, USA) were performed in the remaining 15 patients. Apneic and hypopneic events were scored when minimum event duration of 10 seconds was found. Hypopnea, measured by the nasal cannula, was scored either when a ≥50% reduction of airflow followed by a ≥3% oxygen desaturation or a ≥30% reduction of airflow followed by a ≥4% oxygen desaturation was recorded.[18] In PG, Apnea-hypopnea index (AHI) was defined as the number of apneas/hypopneas during the recording session defined by lights off and lights on. The corresponding AHI in a PSG study was calculated as the number of apneas and hypopneas per hour of total sleep time. The oxygen desaturation index (ODI) was defined as a ≥4% reduction in oxygen saturation.[18] Mild, moderate and severe OSA was diagnosed according to AHI ≥5 – <15, ≥15 – <30 and ≥30 events/hours of sleep,

respectively. Patients not fulfilling the OSA diagnosis based on an AHI ≥5n/h had been diagnosed based on a respiratory disturbance index (RDI, sum of AHI and the Respiratory Effort Related Arousal (RERA) Index) of ≥5/hour (if ESS≥11) (n=11) or a RDI of ≥15/h (n=10).[19]

2.3. Assessment of neurocognitive function

Two different types of neurocognitive tests were performed to assess simple and complex measures of vigilance, sustained attention as well as executive function over time on the day following the sleep study. All patients were comfortably seated in a bed in front of a computer monitor, located in a dark, noise reduced room. The GOSLING,[17] a modified version of the Osler (Gothenburg Oxford SLEep Resistance test)[14], is a simple reaction time test during which sustained attention is assessed over 20 minutes. The patient was instructed to press a computer mouse button in response to a one second low intensity stimulus that appeared on a computer monitor. Each stimulus appeared at random intervals of 3 and 10 seconds to reduce the anticipatory effect. When measuring speed and number of responses to stimuli, simple reaction time (RT, milliseconds (ms)), number of lapses, consecutive number of lapses and total number of responses could be evaluated. A lapse was identified when the response time following a stimulus was >2 seconds and seven consecutive lapses were an indication of sleep onset and the test would automatically be terminate.

The Attention Network Test (ANT)[20, 21] addresses attention related to task fatigue. Three dimensions of attention - alerting, orienting and executive function - are assessed during the 27 minute test. The stimuli presented on the screen are arrows either pointing in the same (congruent >>>>> or <<<<<) or a different (incongruent <<><< or >><>>) direction. The stimulus is either preceded by a cue or no cue. In addition, the location of the cue in relation to the central fixation point varies randomly. The cue can be presented in relation to the location of the upcoming target (spatial), above, below or at the fixation point to alert subjects to when but not where the stimuli could be expected (temporal cue). The alerting effect is measured as RT between no cue and central cue at 400 ms. The difference in RT between spatial and temporal cue measures the orienting effect at 200 ms. Conflict (executive

function) is defined as the difference in RT between congruent and incongruent stimuli and reflects how accurately and efficiently the direction of the arrows are recognized and responded to.[21, 22]

2.4. National traffic accident registry data - STRADA

Individual information on retrospective MVA history between the years 2001 and 2012 was obtained from the Swedish TRaffic Accident Data Acquisition (STRADA)[23] registry. The registry contains nationwide standardized information (>500 000 accidents) reported by the Swedish traffic police at the accident scene and the major emergency hospitals. The present study includes information on MVA and severity of personal injury following the MVA. Patients were cross-analyzed with the STRADA. The number of MVAs per patient and the type of vehicle involved in the accident were obtained.

2.5. Statistics

All statistics were performed by using PASW Statistics 17.0.2 (SPSS Inc. Chicago, USA). Non-parametric independent samples Mann-Whitney U test were used for ordinal scale data as well as for comparison of between group differences. Pearson´s Chi-square was used to assess associations between quantitative data and binary logistic regression was used for categorical response variables and independent categorical as well as continuous predictors. For the best model fit in the logistic regression, stepwise backward and forward likelihood-ratio methods were used to test each predictor, where applicable both as a categorical or a continuous variable. Spearman's rho (r) was used for non-parametric correlation analysis. Data are presented as mean (SD) or median [25th and 75th IQR] and a two tailed P-value <0.05 was considered statistically significant.

3. Results

3.1 Patient characteristics

The study population (n=114, table 1) were predominantly male (74.6%) OSA subjects with a median age of 51.4 [43.0–61.0] years, BMI 30.3[27.4–33.0] kg/m^2, ESS score 11.0[8.0–16.0], AHI and ODI of 24.8[6.0–48.9] n/h and 21.0[5.4 – 40.5] n/h, respectively (table 1). Patients (n=21) with an AHI <5 n/h had a RDI of 10.3[7.2 – 15.8] n/h.

3.2. Motor vehicle accidents

Eleven patients with at least one accident were identified in the STRADA registry (9.6%). MVAs had occurred 3.6(4.8) years prior to the diagnostic sleep test. Seven individuals were commercial drivers (CMDs). Three single accidents and 8 collisions between vehicles were reported. Three accidents (n=2 single accidents) occurred between 21 and midnight, while the rest occurred between 11 and 19. No correlation was found between time of day (day/night) and type of accident (single/collision) (r= -.54, p=0.09). The accidents included drivers of cars (n=6), busses (n=4) and lorry/truck (n=1). Five drivers were mildly injured, no fatality was reported. No between group differences (MVA yes vs. no) were identified in terms of age, BMI, ESS score, and OSA severity (AHI and ODI) (table 2).

3.3. Neurocognitive function in patients with or without MVAs

In the ANT, the median number of lapses was significantly higher, while the total number of responses was lower among patients with MVAs (table 3, figure 1). No significant differences were found in the reaction time (RT) and the number of correct responses, as well as the orienting-, alerting-, or conflicting effects (table 3). In the GOSLING test, the proportion of missed trials (lapses/number of trials), the consecutive and the total number of lapses were significantly higher among patients with MVAs (table 3). In addition, all measures of reaction time (RT), such as median RT (figure 2), interquartile range (IQR) as well as variability, were significantly increased among patients with a previous MVA compared with those without a previous MVA (table 3).

3.4. Independent neurocognitive variables associated with motor vehicle accidents

The GOSLING and the ANT were analyzed in a multivariable logistic regression model adjusted for gender, age, sleep apnea severity (AHI (n/h)) and self-reported EDS (ESS score ≥11) (table 4). In the GOSLING, 10 millisecond increases in median RT, as well as in RT variability were significantly associated with a 13% increased risk of MVAs. Consecutive and total numbers of lapses were associated with a 7.3 and 3.3% increased MVA risk, respectively. Analysis of the ANT showed a 2.3% increased risk of MVAs with each increase in the number of lapses, while decrease in response was associated with a 2.2% increased MVA risk (table 4). RT in the ANT as well as OSA severity (AHI, ODI) and EDS (ESS ≥11) were not associated with MVAs (all $p>0.05$, respectively). In a bivariate Spearman's correlation analysis of OSA severity, OSAS and EDS no significant correlations were found in relation to the GOSLING and ANT test variables (RT, RT variability, number of lapses and responses).

4. Discussion

We have demonstrated that lapses and prolonged reaction times in two neurocognitive function tests was associated with a history of MVA in patients with OSA. To our knowledge, although small, this is the first study to investigate the association between objective measures of cognitive dysfunction and an objective registry defined MVA history in patients with suspected OSA.

Driving is a complex task that requires simultaneous processing of visual information, psychomotor function and sustained attention which may be compromised by EDS. In fact, 20% of traffic fatalities are assumed to be a result from impaired vigilance at the wheel.[24] Several studies have

demonstrated an increased risk of MVA in patients with OSA.[4, 5, 7] Cognitive dysfunction including difficulty to maintain attention and compromised processing of complex information may cause the increased risk of MVA in the OSA population. However, the current and past studies have been unable to demonstrate a clear dose response relation between conventional measures of OSA severity (AHI/ODI) and MVA risk.[4]

Subsequently, several methods have been used to identify patterns of vigilance deficits and neurocognitive dysfunction in the OSA patient population.[25, 26] However, to our knowledge, no attempts have been made to link those deficits to existing objective MVA data. In consequence, no validated routine assessment of daytime dysfunction has been established in OSA management and mostly non-validated algorithms or physician´s subjective arguments are used for ability to drive decisions in OSA patients.

The OSLER test[14] was introduced as an objective and less time consuming test of sleep latency, validated against the MWT.[27] In the current study, we used the GOSLING test,[17] a further development of the validated OSLER test. The advantage of the GOSLING procedure resides in the randomness of the time interval between stimuli. The test was designed to control for the well-known effect of anticipation and automated response reaction which may be maintained in the state of reduced vigilance and sleep wake transitions.[28] Indeed, measures of reaction time, reaction variability, number of lapses of attention were found to differ substantially between patients with or without MVA.

The ANT has been extensively validated in neurocognitive research[22, 29] and against measures of driving capacity.[30, 31] In our study, we used the ANT for the first time, to explore attention with respect to existing MVA history data among OSA patients and we documented that lapses were more frequent in patients with a positive MVA history. This finding suggests that vigilance over time was reduced in OSA patients with a history of MVA which may be explained by factors such as microsleep events, distraction, or more global cognitive impairment as previously described in this subgroup of OSA patients.[25] In addition, mean reaction time in the ANT was longer in patients with MVAs

compared with patients without a MVA history. Although the difference between groups was not significant, patients in the current study exhibited substantially longer reaction times compared to earlier data obtained from healthy subjects suggesting a general slower brain response to a standardized stimulus in the OSA condition.[21, 22] Contrary to our initial hypothesis, three dimensions reflecting functions of alerting, orienting and executive control[20, 29, 32] did not differ in our analysis of OSA patients with and without MVA. When compared to normative data,[30] the orienting and alerting effects found among OSA patients in our study were substantially reduced (mean (SD) orienting 42.4 (37.36) and alerting 33.0 (46.40) in healthy individuals (n=95)[30] vs. 8.3 (74.12) and 18.2 (76.35), respectively, in OSA patients (n=114)). Additionally, the slower reaction time in the ANT conflict effect (executive function) in our study was increased when compared with data from previous studies in healthy individuals (conflict 163.5 (90.02) in healthy individuals[21, 30] vs. 213.7 (150.0) in OSA patients). These findings suggest an overall inhibiting and distracting effect rather than increased alertness following spatial and temporal cues in OSA subjects which may mask the effect of MVA risk prone subjects in our study. In addition, it cannot be excluded that the non-significance in parts of the ANT test performance could be explained by a small sample size. Future studies need to be larger and to include an age matched control group without OSA in order to determine the role of sleep apnea in sustained attention and driver distraction.

Several strength and limitations of our study need to be addressed. The quality of MVA data in the current study is highly robust, as the information was gathered from a nationwide traffic registry based on standardized police reports. The fact that a police officer was required at the scene of the MVA provides a threshold definition of the complexity of the MVA which increases the clinical relevance of the MVA reference material. In the current study we were able to control for many, but not all, factors that might confound the association between markers of cognitive function and MVA history.

The study population included subjects with a wide range of OSA severity and clinical symptoms. Approximately 10% of our patients underwent a PG rather than a PSG sleep study to establish the OSA diagnosis which is likely to cause an underestimation of the degree of OSA.[33] We therefore

replicated the binary logistic regression analysis adjusting for ODI (less sensitive to the sleep test method) as well as an analysis restricted to all patients evaluated by PSG (n=101). The additional analyses all confirmed the predictive value of the ANT and GOSLING parameters stated in table 4. Unfortunately, the limited number of patients with available oxygen saturation below 90% precluded a meaningful analysis. Moreover, complete data on BMI and ODI were missing in 27% and 18%, respectively.

In addition, our study population enriched with professional drivers, 9.6% compared with 5.0% of clinical OSA patients[7], with high traffic exposure may increase the clinical relevance of our findings. Since CMDs are more exposed to traffic and often drive a prolonged period of time, it was not unexpected that the majority of MVAs were observed among CMDs[34-36]. On the other hand, attention deficits, prolonged reaction times, as well as increased number of lapses were not confined to this group. Further, it is recognized that traffic exposure, often assessed as self-reported annual driving distance, represents an important risk factor for MVA [37] which was not assessed in our dataset. However, our study aimed to investigate the feasibility of two neurocognitive function tests to identify OSA drivers at risk for MVA, not to assess general risk factors for MVA in the OSA population. Future large prospective studies are needed to determine the diagnostic capacity of the GOSLING and ANT tests in an unselected OSA population compared with a control population. Finally, it remains unknown to what extent the accidents included in the current analysis were associated with sleepiness and poor attention. However, our findings suggest that accidents involving patients with OSA in fact may be related to sleepiness to a higher degree compared with the general population. In line with previously published studies, the time window for MVA analysis was approximately ±5 years from time of diagnosis and since MVAs are infrequent events a longer observational period is required to calculate MVA risk in this rather small population. A longer observational time window is also justified as OSA is a chronic condition, which usually progresses over several years. Data suggesting that MVA risk may be reduced by OSA treatment[7] provides the

strongest argument for a causal association between on the one hand OSA and neurocognitive deficit, and on the other neurocognitive deficit and MVA risk.

4.1. Conclusion

We have identified attention-related markers of cognitive dysfunction, determined in the ANT and GOSLING tests, in OSA patients with an objectively assessed MVA history. The findings may contribute to the development of objective methods for the identification of OSA-related MVA risk. Further developments including larger and prospective studies evaluated against objectively assessed MVA history are warranted.

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References

1. Lavie P. Incidence of sleep apnea in a presumably healthy working population: a significant relationship with excessive daytime sleepiness. Sleep 1983;6:312-8.

2. Mitler MM. Daytime sleepiness and cognitive functioning in sleep apnea. Sleep 1993;16:S68-70.

3. Mazza S, Pepin JL, Naegele B, Plante J, Deschaux C, Levy P. Most obstructive sleep apnoea patients exhibit vigilance and attention deficits on an extended battery of tests. Eur Respir J 2005;25:75-80.

4. Tregear S, Reston J, Schoelles K, Phillips B. Obstructive sleep apnea and risk of motor vehicle crash: systematic review and meta-analysis. J Clin Sleep Med 2009;5:573-81.

5. George CF. Reduction in motor vehicle collisions following treatment of sleep apnoea with nasal CPAP. Thorax 2001;56:508-12.

6. Masa JF, Rubio M, Findley LJ. Habitually sleepy drivers have a high frequency of automobile crashes associated with respiratory disorders during sleep. American journal of respiratory and critical care medicine 2000;162:1407-12.

7. Karimi M, Hedner J, Häbel H, Nerman O, Grote L. A sleep apnea related excess risk of motor vehicle accident is reduced by CPAP - Swedish Traffic Accident Registry Data. Sleep In press, 2014.

8. Johns MW. Daytime sleepiness, snoring, and obstructive sleep apnea. The Epworth Sleepiness Scale. Chest 1993;103:30-6.

9. Amra B, Dorali R, Mortazavi S, et al. Sleep apnea symptoms and accident risk factors in Persian commercial vehicle drivers. Sleep Breath 2012;16:187-91.

10. Arand D, Bonnet M, Hurwitz T, Mitler M, Rosa R, Sangal RB. The clinical use of the MSLT and MWT. Sleep 2005;28:123-44.

11. Littner MR, Kushida C, Wise M, et al. Practice parameters for clinical use of the multiple sleep latency test and the maintenance of wakefulness test. Sleep 2005 Jan 1;Sect. 113-21.

12. Turkington PM, Sircar M, Allgar V, Elliott MW. Relationship between obstructive sleep apnoea, driving simulator performance, and risk of road traffic accidents. Thorax 2001;56:800-5.

13. Haraldsson PO, Carenfelt C, Laurell H, Tornros J. Driving vigilance simulator test. Acta Otolaryngol 1990;110:136-40.

14. Bennett LS, Stradling JR, Davies RJ. A behavioural test to assess daytime sleepiness in obstructive sleep apnoea. Journal of sleep research 1997;6:142-5.

15. Drummond SP, Bischoff-Grethe A, Dinges DF, Ayalon L, Mednick SC, Meloy MJ. The neural basis of the psychomotor vigilance task. Sleep 2005;28:1059-68.

16. Eskandari D, Zou D, Karimi M, Stenlöf K, Grote L, Hedner J. Zonisamide reduces obstructive sleep apnea: a randomized placebo-controlled study. European Respiratory Journal 2014

17. Karimi M, Eder DN, Eskandari D, Zou D, Hedner JA, Grote L. Impaired vigilance and increased accident rate in public transport operators is associated with sleep disorders. Accident; analysis and prevention 2013;51:208-14.

18. Iber C, Ancoli-Israel S, Quan SF. The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications. 1st ed. Westchester, Illinois: Amercian Academy of Sleep Medicine, 2007.

19. International classification of sleep disorders 3ed. Darien, IL: American Academy of Sleep Medicine, 2014.

20. Fan J, McCandliss BD, Fossella J, Flombaum JI, Posner MI. The activation of attentional networks. NeuroImage 2005;26:471-9.

21. Fan J, Gu X, Guise KG, et al. Testing the behavioral interaction and integration of attentional networks. Brain Cogn 2009;70:209-20.

22. Fan J, McCandliss BD, Sommer T, Raz A, Posner MI. Testing the efficiency and independence of attentional networks. J Cogn Neurosci 2002;14:340-7.

23. STRADA. Swedish Traffic Accident Data Acquisition. 2014 [cited 2014 28 January]; Available from: http://www.transportstyrelsen.se/en/road/STRADA/

24. Akerstedt T. Consensus statement: fatigue and accidents in transport operations. Journal of sleep research 2000;9:395.

25. Bucks RS, Olaithe M, Eastwood P. Neurocognitive function in obstructive sleep apnoea: a meta-review. Respirology 2013;18:61-70.

26. Beebe DW, Groesz L, Wells C, Nichols A, McGee K. The neuropsychological effects of obstructive sleep apnea: a meta-analysis of norm-referenced and case-controlled data. Sleep 2003;26:298-307.

27. Krieger AC, Ayappa I, Norman RG, Rapoport DM, Walsleben J. Comparison of the maintenance of wakefulness test (MWT) to a modified behavioral test (OSLER) in the evaluation of daytime sleepiness. Journal of sleep research 2004;13:407-11.

28. Peter JH, Cassel W, Ehrig B, et al. Occupational performance of a paced secondary task under conditions of sensory deprivation. II. The influence of professional training. Eur J Appl Physiol Occup Physiol 1990;60:315-20.

29. Posner MI, Rothbart MK. Research on attention networks as a model for the integration of psychological science. Annu Rev Psychol 2007;58:1-23.

30. Weaver B, Bedard M, McAuliffe J, Parkkari M. Using the Attention Network Test to predict driving test scores. Accident; analysis and prevention 2009;41:76-83.

31. Edwards JD, Ross LA, Wadley VG, et al. The useful field of view test: normative data for older adults. Arch Clin Neuropsychol 2006;21:275-86.

32. Posner MI, Petersen SE. The attention system of the human brain. Annu Rev Neurosci 1990;13:25-42.

33. Escourrou P. Polygraphy or PSG - how does the procedure influence diagnosis and management. In: 21st Congress of the European Sleep Research Society Paris, France, 2012.

34. McCartt AT, Rohrbaugh JW, Hammer MC, Fuller SZ. Factors associated with falling asleep at the wheel among long-distance truck drivers. Accident Analysis & Prevention 2000;32:493-504.

35. Stoohs RA, Guilleminault C, Itoi A, Dement WC. Traffic accidents in commercial long-haul truck drivers: the influence of sleep-disordered breathing and obesity. Sleep 1994;17:619-23.

36. Sagberg F. Road accidents caused by drivers falling asleep. Accident Analysis & Prevention 1999;31:639-49.

37. Karimi M, Hedner J, Lombardi C, et al. Driving habits and risk factors for traffic accidents among sleep apnea patients - a European multi-centre cohort study. Journal of sleep research 2014.

Figure 1. The boxplot illustrates the number of lapses (ANT) in patients with or without a motor vehicle accident (MVA).

Statistics: The boxplot illustrates the median, 25th and 75th percentiles, and the whiskers represent the highest and lowest values. Outliers represent values °≥1.5 or *≥3 ranges away from the 75th percentile.

Figure 2. The boxplot illustrates the number of lapses (GOSLING) in patients with or without a motor vehicle accident (MVA).

Statistics: The boxplot illustrates the median, 25th and 75th percentiles, and the whiskers represent the highest and lowest values. Outliers represent values °≥1.5 or *≥3 ranges away from the 75th percentile.

Table 1. Characteristics of the three sub-cohorts included in the main study cohort (n=114).

	Sub-cohort I N=58	Sub-cohort II N=43	Sub-cohort III N=13	P-value	All N=114
Male, n (%)	34 (58.6)	40 (93.0)	11 (84.6)	0.001	85 (74.6)
Age, yrs	53 [44 – 62]	53 [42 – 61]	53 [42 – 56]	0.8	51 [43 – 61]
BMI, kg/m^2	28 [25 – 33]	31 [29 – 33]	28 [26 – 33]	0.1	30 [27 – 33]
AHI, n/h	11 [2 – 34]	43 [26 – 62]	18 [12 – 35]*	<0.001	25 [6 – 49]
ODI, n/h	8 [1 – 27]	35 [22 – 61]	13 [5 – 30]	<0.001	21 [5 – 41]
ESS score	12 [7 – 16]	12 [9 – 17]	9 [4 – 13]	0.08	11 [8 – 16]
MVA, n (%)	8 (14)	2 (5)	1 (8)	0.2	11

Statistics: Data are presented as median [IQR]. Non-parametric Mann-Whitney U test and Pearson Chi-square test were used for between group differences. *AHI based on PG recording.
Abbreviations: BMI = Body Mass Index, AHI = Apnea-Hypopnea Index, ODI = Oxygen Desaturation Index, ESS = Epworth Sleepiness Scale, MVA = Motor Vehicle Accident.

Table 2. Clinical data in patients with or without a history of motor vehicle accident (MVA).

	MVA (n=11) Median [IQR]	No MVA (n=103) Median [IQR]	P-value
Gender (Male), n (%)	8 (73)	77 (75)	0.8

Age, yrs	56 [49 – 62]	52 [43 – 61]	0.4
BMI*, kg/m^2	28 [25 – 30]	31 [28 – 33]	0.1
ESS score	9 [3 – 18]	11 [9 – 16]	0.4
ESS score ≥ 11, n (%)	6 (54.5)	74 (72)	0.2
AHI, n/h	20 [5 – 58]	25 [6 – 48]	0.9
ODI, n/h**	26 [7 – 49]	21 [3 – 38]	0.7
OSA, (AHI ≥5 n/h), n %	8 (73)	80 (78)	0.7
CMD, n (%)	7 (64)	28 (27)	0.01

Statistics: Data are presented as median [IQR]. Non-parametric Mann-Whitney U test and Pearson Chi-square test were used for between group differences. Data completeness: *73%, **82%.
Abbreviations: BMI = Body Mass Index, ESS = Epworth Sleepiness Scale, AHI = Apnea-Hypopnea Index, ODI = Oxygen Desaturation Index, OSA = Obstructive Sleep Apnea, CMD = Commercial Driver.

Table 3. Neurocognitive parameters assessed by the ANT and GOSLING tests in patients with or without a motor vehicle accident (MVA).

ANT	**Total (n=114) MVA/No MVA**	**MVA (n=11)**	**No MVA (n=103)**	**P-value**
Lapse, n	11/103	42 [5 – 121]	5 [1 – 25]	0.02
Response, n	11/103	238 [158 – 272]	271 [256 – 277]	0.03
RT, ms	11/103	924 [736 – 1000]	844 [745 – 960]	0.4
RT IQR, ms	10/95	282 [197 – 481]	259 [177 – 459]	0.7
Correct, n	11/103	232 [155 – 271]	263 [234 – 275]	0.1
Orienting RT, ms	11/103	4 [-49 – 51]	11 [-28 – 48]	0.9
Alerting RT, ms	10/103	9 [-46 – 37]	23 [-20 – 60]	0.4
Conflict RT, ms	8/102	199 [112 – 289]	208 [146–294]	0.7
GOSLING	**Total (n=92) MVA/No MVA**	**MVA (n=9)**	**No MVA (n=83)**	**P-value**
Lapses, n	9/83	29 [10 – 97]	7 [2 – 19]	0.01
Consec. lapses, n	9/83	15 [8 – 45]	6 [2 – 14]	0.03
Missed trials, %	9/83	0.2 [0.03 – 0.31]	0.02 [0.01 – 0.06]	0.01
Median RT, ms	9/83	462 [393 – 551]	407 [361 – 449]	0.05
RT variability, ms	9/80	512 [415 – 580]	448 [387 – 495]	0.04
RT IQR, ms	9/83	175 [103 – 200]	112 [84 – 141]	0.03

Statistics: Data are presented as median [IQR]. Non-parametric Mann-Whitney U test and Pearson Chi-square test were used for between group differences.
Abbreviations: ANT=Attention Network Test, RT=Reaction Time, ms=millisecond, Consec.=Consecutive, IQR=Inter Quartile [25th -75th] Range.

Table 4. Neurocognitive parameters in the GOSLING and the Attention Network Test associated with motor vehicle accident (MVA, yes/no).

	Estimate (S.E)	**OR**	**95% CI**	**P-value**
ANT (n=114)				
Lapses, n	**0.022 (0.007)**	**1.023**	**1.009 – 1.037**	**0.01**
Constant	-4.76 (2.12)			0.02

Response, n	**-0.022 (0.007)**	**0.978**	**0.965 – 0.991**	**0.001**
Constant	1.36 (2.14)			0.5
RT, ms	**0.003 (0.002)**	**1.003**	**0.999 – 1.007**	**0.2**
Constant	-4.80 (2.24)			0.03
GOSLING (n=92)				
Lapse, n	**0.033 (0.013)**	**1.033**	**1.008 – 1.060**	**0.01**
Constant	-6.01 (2.48)			0.01
Consec. lapses, n	**0.07 (0.03)**	**1.073**	**1.014 – 1.135**	**0.01**
Constant	-5.95 (2.41)			0.01
Median RT, ms	**0.013 (0.005)**	**1.013**	**1.002 – 1.023**	**0.02**
Constant	-8.81 (3.04)			0.003
RT variability, ms	**0.013 (0.01)**	**1.013**	**1.002 – 1.024**	**0.02**
Constant	-9.54 (3.35)			0.004

Statistics: All variables are adjusted for gender, age (years), ESS score ≥11 (yes/no) and AHI (n/h). P<0.05 was considered significant.

Abbreviations: ANT=Attention Network Test, RT= Reaction Time, ms=millisecond, Consec.=Consecutive.